Zydus Lifesciences announces completion of Enrolment for Phase II clinical trial of Usnoflast, a novel oral NLRP3 inflammasome inhibitor in patients with Amyotrophic Lateral Sclerosis (ALS)

- *ALS is a rare, progressive and fatal neurodegenerative disease, with an average life expectancy of 3 to 5 years from the time of symptom onset.*
- *The Phase 2 clinical trial will assess the safety and efficacy of Usnoflast in ALS patients [ClinicalTrials.gov ID: NCT05981040]*

Ahmedabad, India, 24 May, 2024

Zydus, a leading discovery-based, global pharmaceutical company, announced today that it has completed enrolment of its Phase II clinical study of NLRP3 inhibitor 'Usnoflast (ZYIL1)' in patients with Amyotrophic Lateral Sclerosis (ALS).

ALS patients experience neuroinflammation and rapid neurodegeneration leading to steady loss of the ability to move, speak, eat and eventually breathe. ALS results in loss of motor neurons in the brain and spinal cord which controls voluntary muscle movement. ALS affects approximately 31,000 people in the U.S.A and on an average 5,000 new patients are diagnosed every year with this disease in USA as per statistics from Centers for Disease Control and Prevention (CDC). More than 30,000 people are estimated to be living with ALS in Europe (European Union and United Kingdom), while India has an estimated 75,000 people living with ALS. People living with ALS have a median survival of approximately two years from diagnosis.

The Phase II clinical trial has recruited 24 ALS patients across 7 clinical trial sites in India and will study safety, tolerability, pharmacokinetics and pharmacodynamics of Usnoflast. The change from baseline in the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) score will be measured at week 4, week 8 and week 12, as the trial's primary endpoint is the placebo-controlled, randomised, double-blind Phase 2 clinical trial. The trial will also evaluate Key Secondary Endpoints including Slow Vital Capacity (SVC), a predictor of functional loss in ALS and neurofilament levels at week 4 and week 12.

Usnoflast (ZYIL1) is a novel, oral small molecule NLRP3 inhibitor. Studies have demonstrated that ZYIL1 is highly potent in human whole blood assay and can suppress inflammation caused by the NLRP3 inflammasome. Usnoflast was found distributed in the brain and CSF of various nonclinical species including mice, rats and non-human primates. The efficacy of Usnoflast has been established in several validated pre-clinical models of neuroinflammation, Parkinson's disease, Inflammatory Bowel Disease (IBD) and Multiple Sclerosis (MS). The candidate, Usnoflast, has an acceptable ADME profile, with a good safety margin. In Phase I studies, Usnoflast was found to be safe and well-tolerated

PRESS RELEASE

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[NCT04731324, NCT04972188]. Zydus has initiated a Phase 2 clinical study of Usnoflast in Ulcerative Colitis [ClinicalTrials.gov ID NCT06398808]. Zydus has established the Phase 2 proof-of-concept in CAPS patients [NCT05186051] and has now published the data in Clinical Pharmacology in Drug Development. The USFDA has granted Zydus an 'Orphan Drug Designation' for Usnoflast to treat patients with Cryopyrin Associated Periodic Syndrome (CAPS), a rare auto-inflammatory disease.

References:

1. ClinicalTrials.gov Identifier: NCT04972188 A Phase I, Prospective, Open Label, Multiple Dose Study of ZYIL1 Administered Via Oral Route to Investigate The Safety, Tolerability, Pharmacokinetics And Pharmacodynamics In Healthy Adult Subjects
2. ClinicalTrials.gov Identifier: NCT04731324 A Phase 1, Prospective Open Label, Single Dose, Single Arm Study of ZYIL1 Administered Via Oral Route to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Healthy Adult Human Subjects
3. ClinicalTrials.gov Identifier: NCT05186051 A Phase 2a, Prospective, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ZYIL1 in Subjects With Cryopyrin Associated Periodic Syndromes (CAPS)
4. ClinicalTrials.gov ID NCT06398808 A Study to Evaluate the Efficacy and Safety of ZYIL1 Oral Capsules for the Treatment of Patients With Mild to Moderately Active Ulcerative Colitis Resistant or Intolerant to Oral Aminosalicylates
5. ClinicalTrials.gov ID NCT05981040 A Phase 2, Proof-of-concept, Placebo Controlled, Randomized, Multi-centre, Double Blind Study of ZYIL1 to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Patients With Amyotrophic Lateral Sclerosis (ALS)
6. Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of the Oral NLRP3 Inflammasome Inhibitor ZYIL1: First-in-human Phase 1 studies (Single Ascending Dose and Multiple Ascending Dose), Clinical Pharmacology in Drug Development, 2022. DOI: 10.1002/cpdd.1162
7. Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ZYIL1 in Three Patients with Cryopyrin-Associated Periodic Syndromes, Clinical Pharmacology in Drug Development, 2023, 0(0) 1–8. DOI: 10.1002/cpdd.1318.

About Zydus

Zydus Lifesciences Ltd. with an overarching purpose of empowering people with freedom to live healthier and more fulfilled lives, is an innovative, global lifesciences company that discovers, develops, manufactures, and markets a broad range of healthcare therapies. The group employs over 26,000 people worldwide, including 1,400 scientists engaged in R & D, and is driven by its mission to unlock new possibilities in lifesciences through quality healthcare solutions that impact lives. The group aspires to transform lives through pathbreaking discoveries. Over the last decade, Zydus has introduced several innovative, first-in class products in the market for treating unmet healthcare needs with vaccines, therapeutics, biologicals and New Chemical Entities. For more details visit www.zyduslife.com

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